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| 10/525,453 | 02/18/2005 | Karsten Reihs | 785-012125-US (PAR) | 5072 |
| 2512 | 7590 | 04/01/2009 | EXAMINER | |
| PERMAN & GREEN 425 POST ROAD FAIRFIELD, CT 06824 | | | WHITE, DENNIS MICHAEL | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|---------------------------------------|--|
| Office Action Summary | Application No. 10/525,453 | Applicant(s) REIHS, KARSTEN | |
| | Examiner DENNIS M. WHITE | Art Unit 1797 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 January 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 and 17-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 and 17-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Amendments filed on 1/26/2009 are noted. Claims 1-2, 4-6, 8, 10-11, 17-19 are amended. Claims 13-16 are cancelled. Currently claims 1-12 and 17-20 are pending.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. Claims 1-7, 10-12, 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beecher et al (WO 00/67293) in view of Dreyfus (USP 5,854,486).

Regarding claim 1, Beecher et al teach a MALDI sample carrier with a surface formation with a multitude of MALDI matrix points, characterised in that the MALDI matrix points are deposited ("applied to the sample carrier") from the liquid phase (Pg. 11 lines 4-15). Beecher et al teach the polytrifluoroethylene film ("surface formation has a first layer with an ultraphobic surface") and substrate layers ("carrier layer" "several layers") (Figure 1: 101 and 102) applied by screen printing, electrospray, and making the area prior to deposition ("applied reversibly on a carrier layer"). Beecher et al. teach the thickness is preferably 100 microns thick (Pg. 7 line 30). Beecher et al teach the Beecher et al is silent about the MALDI matrix is applied by precipitation of a MALDI matrix substance from the gas phase, preferably by sublimation and the deviation is <100 micrometers over 100mm.

Dreyfus teaches a MALDI sample carrier in which the matrix material is deposited from the gas phase on to a substrate by sublimation. The film 20 is preferably thicker than 1 nm, more preferably thicker than 10 nm, and most preferably thicker than 100 nm which allows efficient use of the laser light to desorb the film. As the

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films grown thicker than 1 micron, the surface becomes rougher. However, the method may still be used to produce films 20 of 10 microns and thicker. The thickness uniformity of the film across the area to be illuminated by laser beam 4 is preferably more uniform than $\pm 50\%$, and most preferably more uniform than $\pm 10\%$ of the average film thickness. If the variation is 10% with the thickness of the film is 10 microns, the deviation would be 1micron which reads on the claimed deviation of <100 micrometers. It is desirable to deposit the matrix material by sublimation from the gas phase because it provides pinhole free layers and the ability to vary the seed crystal density (col. 4 lines 26-51). It is desirable to provide the film with a uniform thickness more uniform than $\pm 10\%$ as pointed out by Dreyfus (col. 4 lines 46).

Therefore it would have been obvious to one of ordinary skill in the art to perform the depositing step of Beecher by using the known step of depositing by sublimation of the gas-phase MALDI matrix because it provides pinhole free layers and the ability to vary the seed crystal density.

Therefore it would have been obvious to one of ordinary skill in the art, as motivated by Dreyfus to provide the film with uniform thickness more uniform than $\pm 10\%$ of the thickness of the Beecher film (which is 100 microns thick, therefore reading on the deviation is less than 100 micrometers) in order that the whole surface is covered with the matrix.

Regarding claim 2, Beecher/Dreyfus teach manufacturing the film above wherein the film ("plate") (Figure 1:102) covers the substrate ("sample carrier") (Figure 1:101) during the precipitation from the gas phase, which has openings ("plate has through

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holes whose cross-sectional area corresponds to the cross-sectional area of the respective MALDI matrix points”) where the matrix is deposited (Pg. 11 lines 4-15).

Regarding claims 3-5, Beecher/Dreyfus teach that the film has a plurality of openings that are arranged in an orderly fashion for easy addressability (“plate has at least one further through hole by means of which information is transferred to the sample carrier by precipitation of the MALDI matrix substance from the gas phase” “alignment points” “MALDI matrix points are arranged along a grid”) (Pg. 8 lines 7-8).

Regarding claim 6, Beecher/Dreyfus teach the openings can comprise both affinity surface to capture the analyte and adding the energy absorbing material (“MALDI matrix points have substructures”) (Pg. 2 lines 6-8).

Regarding claim 7, Beecher/Dreyfus teach the openings containing the MALDI matrix points are separated into several partial points, preferably isolated from one another (Figure 1: 103).

Regarding claim 10, Beecher/Dreyfus teach the matrix comprises cinnamic acid derivatives such as .alpha.-cyano-4-hydroxycoumarin acid (Pg. 5 lines 31-34 and Hutchens et al USP 5,719,060 col. 6 lines 30-35).

Regarding claim 11-12, Beecher/Dreyfus teach the film comprises polymers such as polytrifluoroethylene and the matrix is cinnamic acid (“characterised in that the sample carrier has an ultraphobic surface” “characterised in that the MALDI matrix points or partial points represent hydrophilic areas which are completely surrounded by ultraphobic areas”) (Beecher: Pg. 5 line 31, Pg. 8 lines 19-28 and Figure 1:103, 101).

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Regarding claim 14, Beecher/Dreyfus teach device has a The maximum local flatness deviation of the surface formation on a length of 100 mm would intrinsically be <100 μm .

Regarding claim 17, Beecher/Dreyfus teach the film can be epoxy resin (“characterised in that the first layer is glued to the carrier layer”) (Pg. 9 lines 1-5).

Regarding claim 18, Beecher/Dreyfus teach the film and substrate can be electrically conducting (“characterised in that there is an electrical contact between the first layer and the carrier layer”) (Pg. 6 line 17 and claim 5 line 1).

Regarding claim 19, Beecher/Dreyfus teaches a laser desorption time of flight mass spectrometer used with a probe comprising a film of self-assembled monolayer for example decane thiol on gold (“consisting of material impervious to water vapour and, preferably, impervious to light”) and MALDI matrix in the openings wherein the probe is in a vacuum chamber (“surrounded by a hollow body containing a vacuum”) (Pg. 10 lines 10-17).

Regarding claim 20, Beecher/Dreyfus teaches the openings or feature comprises binding functionalities such as antibodies (“additional biological material on the MALDI matrix point”) (Pg. 5 lines 7-15 and Pg. 12 claim 7).

4. Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beecher et al (WO 00/67293) in view of Dreyfus (USP 5,854,486) and further in view of Nelson et al (USP 5,955,729).

Regarding claim 8, Beecher/Dreyfus teach the use of MALDI matrix such as cinnaminic acid derivatives, sinapinic acid and dihydroxybenzoic acid. Beecher/Dreyfus are silent about different MALDI matrix substances are applied to a sample carrier.

Nelson et al teach a method of identifying captured analytes using laser desorption/ionization in which same or different suitable MALDI matrix or matrices may be applied to the surfaces (col. 9 line 57-col. 10 line 23). It is desirable to use suitable MALDI matrix materials for analytes that differ in size.

Therefore it would have been obvious to one of ordinary skill in the art to apply different MALDI matrix substances to the sample carrier for the above advantages.

Regarding claim 9, Beecher/Dreyfus/Nelson teach the matrix in the openings ("that at least several MALDI matrix points or partial points each consisting of one MALDI matrix substance are built up").

Response to Arguments

5. Applicant's arguments, with respect to the rejection under 35 U.S.C. 112, first paragraph, of claim 10 and the rejection of claims 1-20 under 35 U.S.C. 112, second paragraph, in light of the claim amendments have been fully considered and are persuasive. Therefore the rejections of these claims have been withdrawn.

6. Applicant's arguments with respect to claims 19-20 have been considered but are moot in view of the new ground(s) of rejection.

7. Regarding the rejections of claims 1-12 and 17-20 under 35 U.S.C. 103, applicant's arguments filed on 1/26/2009 have been fully considered but they are not persuasive. Applicants argue that the limitation that the local flatness deviation of the

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surface formation on a length of 100 mm is neither disclosed nor suggested by Beecher et al. or Dreyfus et al, and Beecher et al. discusses thickness at page 7 lines 26-30 of his specification but does not even mention uniformity. It is noted that Beecher et al teach the film is 100 microns thick. Dreyfus et al teach the claimed deviation in describing the uniformity as per the above rejections. Therefore Beech in view of Dreyfus does teach the local flatness when describing the uniformity of the matrix. Applicants argue that because the amount of deviation allowed by Dreyfus et al. is not considered a significant factor in his product or process is basis that Dreyfus does not teach the limitation. This is not convincing because the claimed limitation is taught by Dreyfus as per above and Dreyfus teaches it is more preferable to have a deviation of less than 10%. Regarding the deviation, the combination of Beecher in view of Dreyfus uses the sublimation in Dreyfus and therefore would cause the matrix to be uniform and therefore the combination of Beecher in view of Dreyfus meet the claimed limitations.

Conclusion

8. No claims are allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within

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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DENNIS M. WHITE whose telephone number is (571)270-3747. The examiner can normally be reached on Monday-Thursday, EST 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Lyle A Alexander/

Primary Examiner, Art Unit 1797

/dmw/